

SALUS: Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies

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SRDC Ltd, AGFA Healthcare

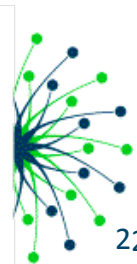
Convergence Meeting: Semantic Interoperability for Clinical
Research & Patient Safety in Europe

SALUS: Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies (<http://www.salusproject.eu/>)

- A STREP funded under Objective ICT-2011.5.3b) Tools and environments enabling the re-use of electronic health records which aims to
 - Enable effective integration and utilization of electronic health record (EHR) data to improve post-market safety activities on a proactive basis
 - Build the necessary interoperability architecture for enabling ADE detection tools, signal validation and strengthening processes and real time screening of multiple, distributed, heterogeneous EHRs for early detection of adverse event signals
 - Enable semantic interoperability for reuse of EHRs in drug safety research
 - Build novel framework for open-ended temporal pattern discovery on top of the electronic health records
 - Ensure security and privacy
 - Pilots in Lombardia Region (Italy) and Eastern Saxony (Germany)

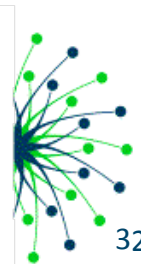
▶ **Partners**

- | | |
|----------------------------------|----------------------|
| ▶ SRDC Ltd, Turkey (coordinator) | ▶ ERS, Netherlands |
| ▶ EUROREC, France | ▶ LISPA, Italy |
| ▶ WHO- UMC, Sweden | ▶ INSERM, France |
| ▶ OFFIS, Germany | ▶ TUD, Germany |
| ▶ AGFA Healthcare, Belgium | ▶ ROCHE, Switzerland |

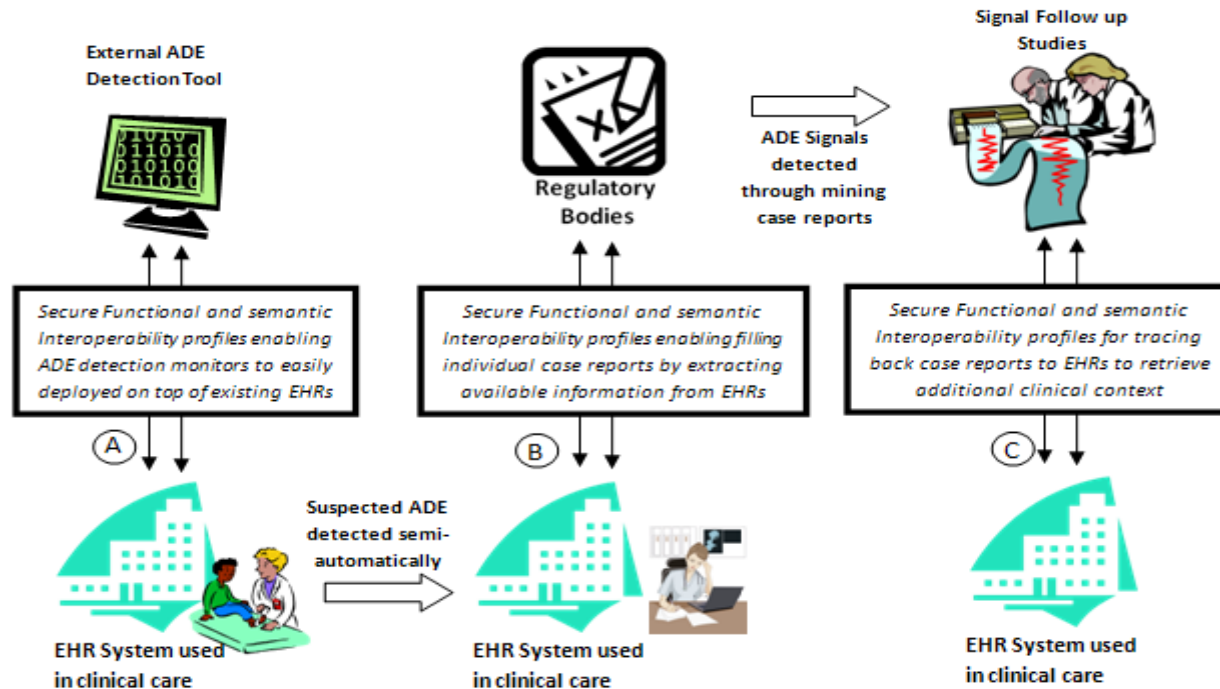


Objectives

- Address the interoperability gap between clinical care and research domains:
 - Use of electronic health record (EHR) data to improve post-market safety activities on a proactive basis
 - EHR covers extended parts of the underlying medical histories, include more complete information on potential risk factors, and not restricted to patients who have experienced a suspected ADE
 - Denominator is missing in SRS data
- Aim to create the necessary infrastructure to enable secondary use of EHRs in an efficient and effective way for reinforcing the post market safety studies

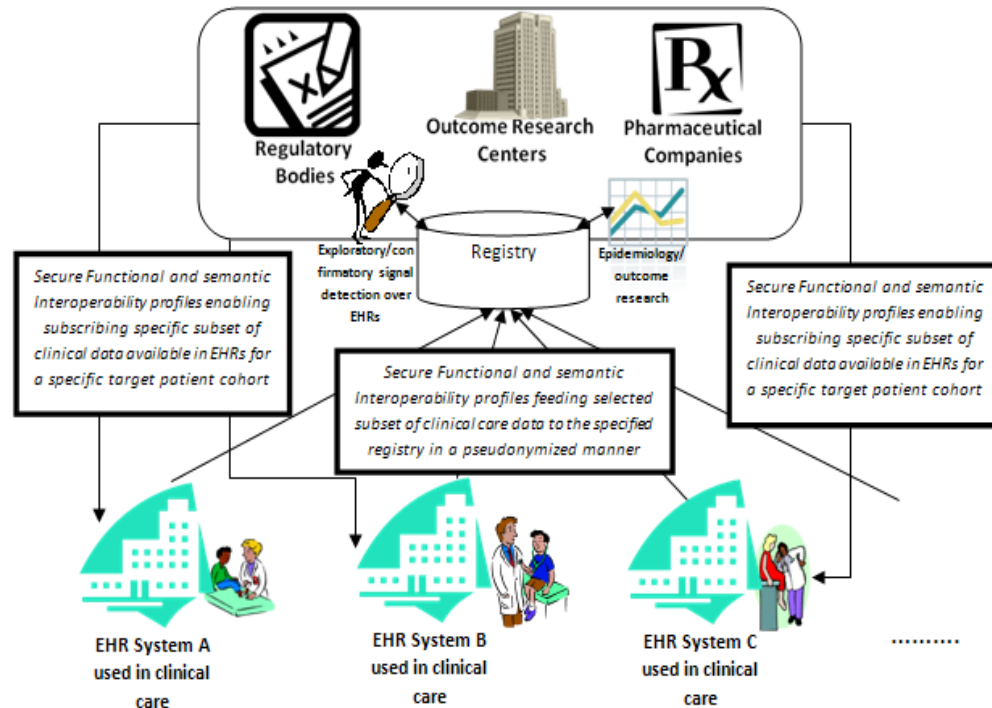


How SALUS extends current spontaneous reporting system to seamlessly exploit the already existing clinical data at EHRs



An ideal system for ADR surveillance would combine the strengths of case reports with those of EHRs

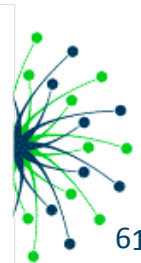
How SALUS enables exploratory/confirmatory signal detection and epidemiological research studies on top of heterogeneous EHRs



- Screening of heterogeneous EHR data for adverse event signals detection
- Carrying out outcome research to identify long term effects of drugs

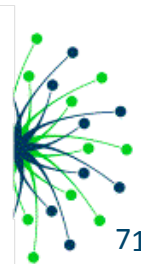
Selected Use Cases

- Enabling Semi-automatic Notification of Suspected ADEs and Reporting ADEs within a Hospital
 - Enabling Notification of Suspected ADEs
 - Enabling Semi-automatic ADE Reporting
- Supporting Clinical Evaluation of a Potential Signal through Accessing the EHRs
 - Characterizing the cases and contrasting them to a background population
 - Temporal pattern discovery
- Running Exploratory Analysis Studies over EHRs for Signal Detection
 - Temporal association screening on EHRs
 - Manual clinical review of relevant medical history
- Using EHRs as secondary use data sources for Post Marketing safety studies
 - Estimate incidence rates of CHF in diabetic patients with a recent acute coronary syndrome (ACS) event on different diabetic medications



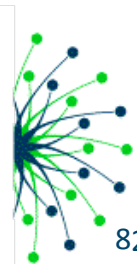
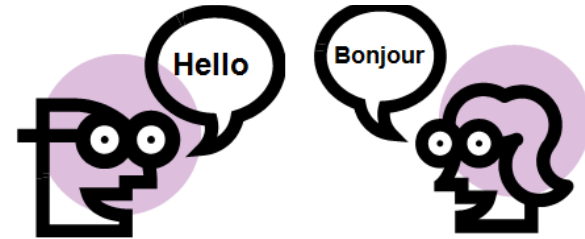
Characterizing the cases and contrasting them to a background population

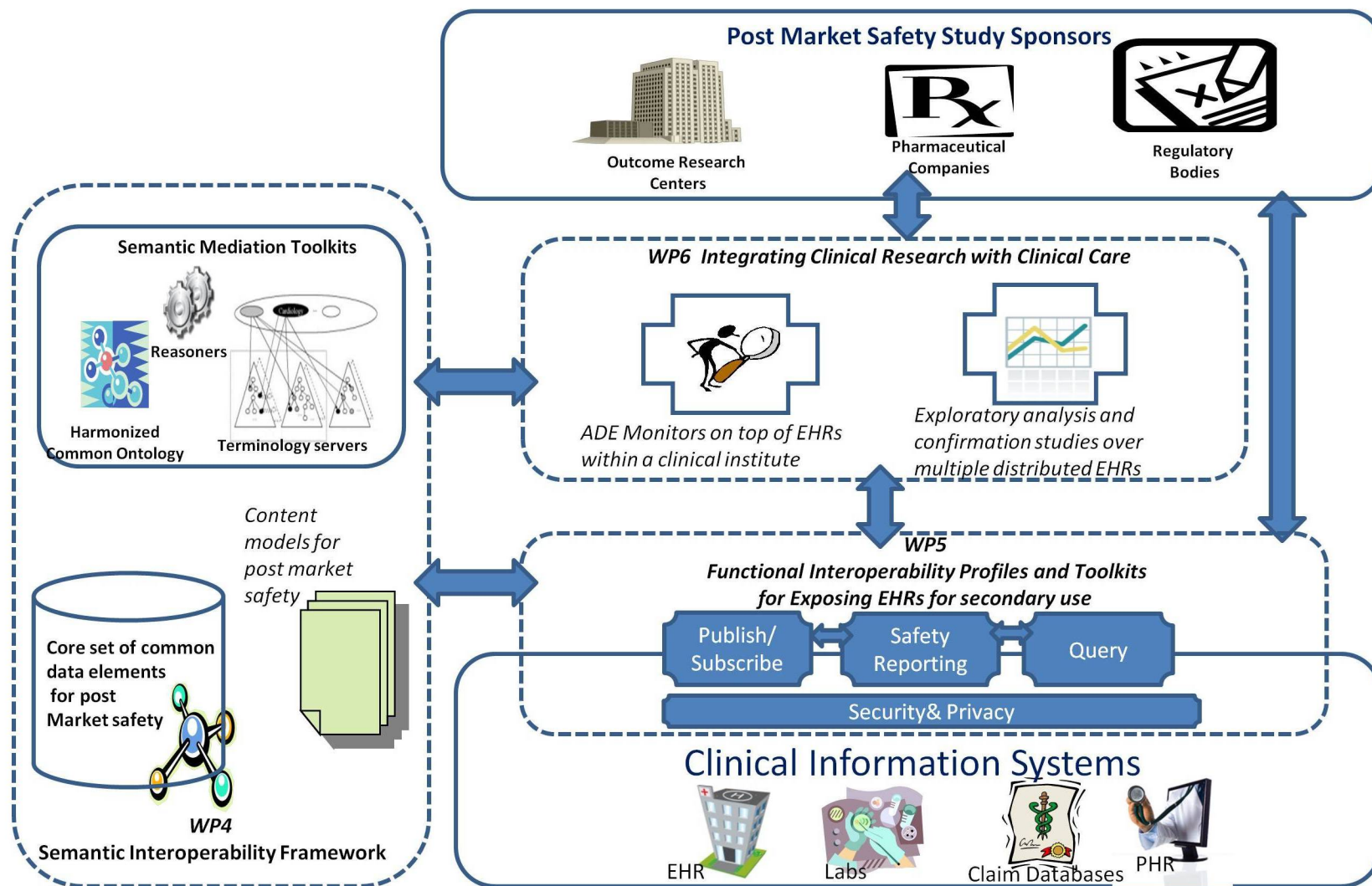
- During investigation of Nifedipine and myocardial infarction at the Uppsala Monitoring Centre 20 out of 82 cases were found to originate from SALUS connected health facilities
 - The analyst logs in to SALUS as an authorized user validated to see summarized statistics from the health care facility data connected through the SALUS architecture
 - The query is sent through the SALUS framework specifying that summarized statistics for Nifedipine and myocardial infarction contrasted against Nifedipine in general is to be returned
 - SALUS automatically highlights events and covariates that are substantially more (or less) common in patients with myocardial infarction after Nifedipine than in patients on Nifedipine in general. This allows the analyst to:
 - Identify potential risk factors and confounders like age, smoking/alcohol habits, prior prescriptions of other medications associated with medical conditions such as diabetes etc.
 - Find predisposing factors and co-morbid conditions like deep vein thrombosis indicating cardiovascular disease by comparing the medical events prior to the medical event of interest for the 20 cases to the medical events occurring in close relation to the drug prescription for all patients.
 - Characterize the outcome and course of the disease by looking at the events occurring after the medical event in question.



Challenges to be addressed in SALUS

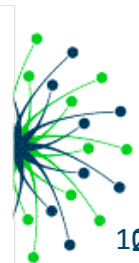
- The problem of Interoperability
 - Syntactic and Semantic
- The ability to exchange information
 - access
- The ability to use the information once it has been exchanged
 - understand
- Security and privacy
- Intelligent tools to analyze the collected content





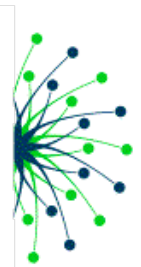
Technical Interoperability

- Achieving syntactic and functional interoperability between EHR Systems and clinical research systems
 - (1) to seamlessly query heterogeneous EHR systems for analysing and detecting possible ADEs, pre-filling case safety reports and for enabling signal follow-up studies to trace the safety reports back to the related EHRs
 - (2) to seamlessly specify the target eligible patient group for enabling set up of continuous safety studies that screen EHRs
 - (3) to specify the requested clinical data by intelligent data analysis tools for the selected group of patients
 - (4) to transfer the specified de-identified clinical data to the clinical data registries for the selected patients for safety analysis
 - Transaction definitions!
 - Content agnostic
- ▶ SALUS WP5: Functional Interoperability Toolkits for secondary use of EHRs in Post Market Safety Studies
 - ▶ Task 5.1 Subscription Based Interoperability Profiles and Open Source Toolsets
 - ▶ Task 5.2 Query Based Interoperability Profiles and Open Source Toolsets
 - ▶ Task 5.3 Interoperability Profiles and Open Source Toolsets for Reporting Activities for Post Market Safety Studies



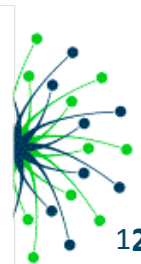
Proposed Approach

- Two complementary approaches will be followed:
 - By providing a semantic interoperability layer on top of the functional interoperability profiles to be developed in WP5: clinical research and clinical care systems can communicate through using well accepted standards like HL7 CDA, CEN EN 13606 archetypes, and CDISC ODMs within the scope of well defined transactions, yet be able to meaningfully interpret these syntactically different but semantically similar content models
 - By enabling the development of semantic interfaces on top of the clinical information sources, so that clinical data exchange among clinical care and research systems can be handled based on a common semantic model
- Provide a migration path from clinical care and research systems that can communicate through semantically enhanced functional interoperability profiles to clinical care and research systems that support full-fledged semantic systems enabling semantic interfaces through our harmonized patient safety ontology.



Current Progress in WP5

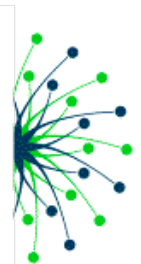
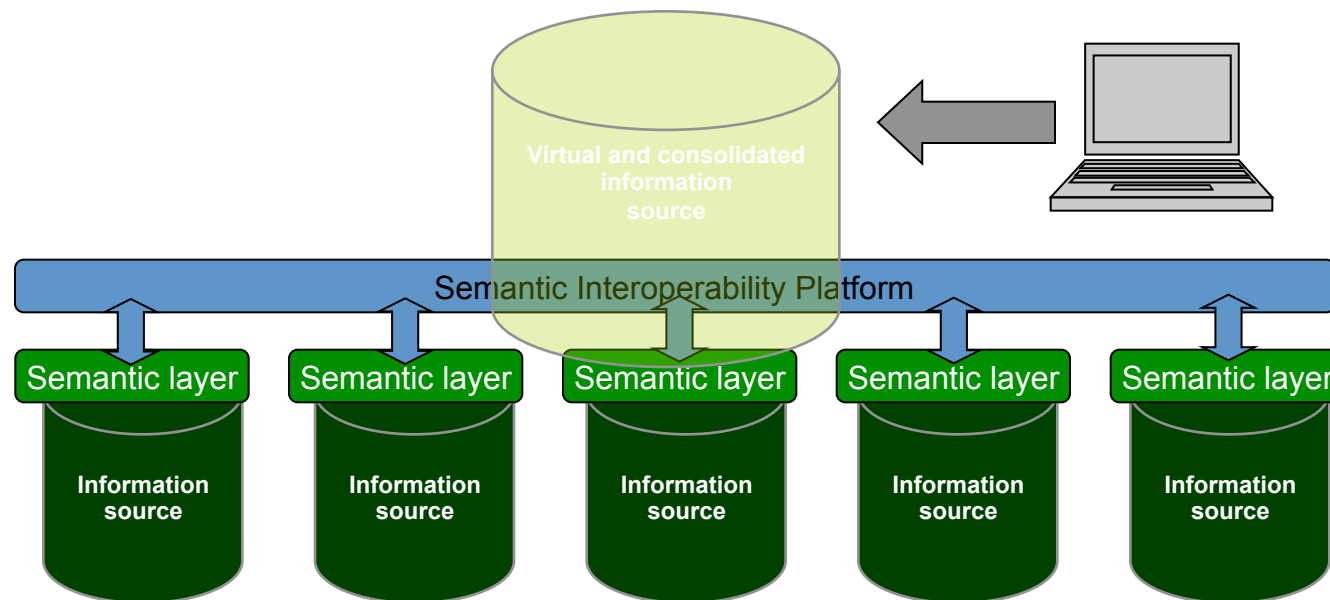
- Tasks 5.1 & 5.2 (Subscription/Query Based Interoperability Profiles)
 - Related available interoperability approaches have been examined
 - HL7 CRFQ
 - IHE QRPH Profiles: IHE RFD, IHE CRD
 - Form based interaction, not query/subscription based, focusing on case safety reports
 - IHE PCC Profiles: IHE QED, IHE CM
 - Subscription/query based, yet not specialized for population based queries
 - Representing eligibility queries:
 - HL7 HQMF queries
 - HL7 Study Design Message
 - Now, the Consortium is working on the extensions to IHE QED and CM Profiles to pass population based queries
 - In parallel with this, we will be actively involved in IHE DEX Profile as co-author
 - Exploitation of metadata registries for flexible mapping of medical summaries to research data required by Clinical research systems (like CRF forms, safety reports)
 - Based on our IEEE TITB publication...



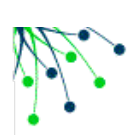
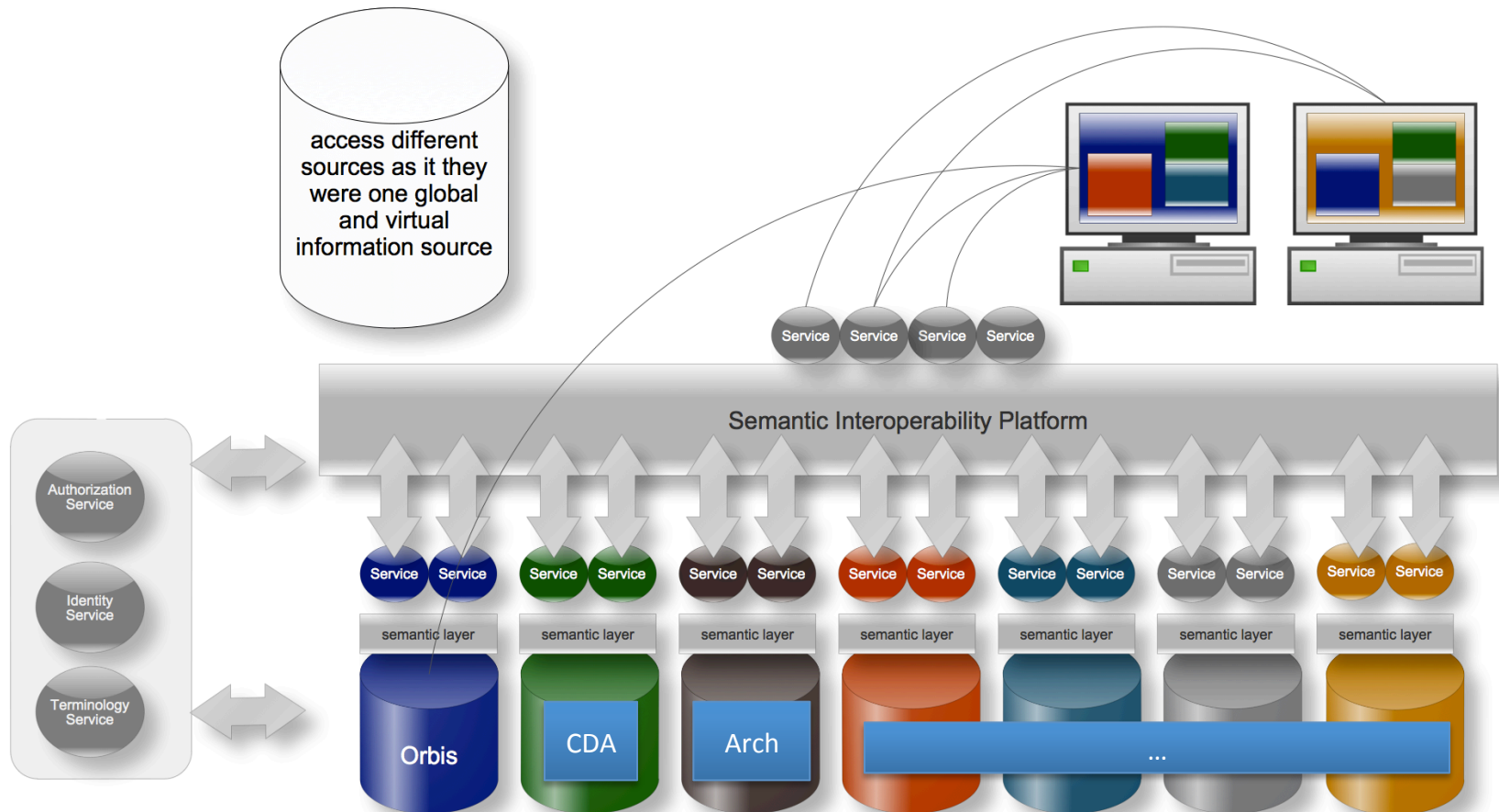
Introduction

The Semantic Interoperability Platform (SIP)

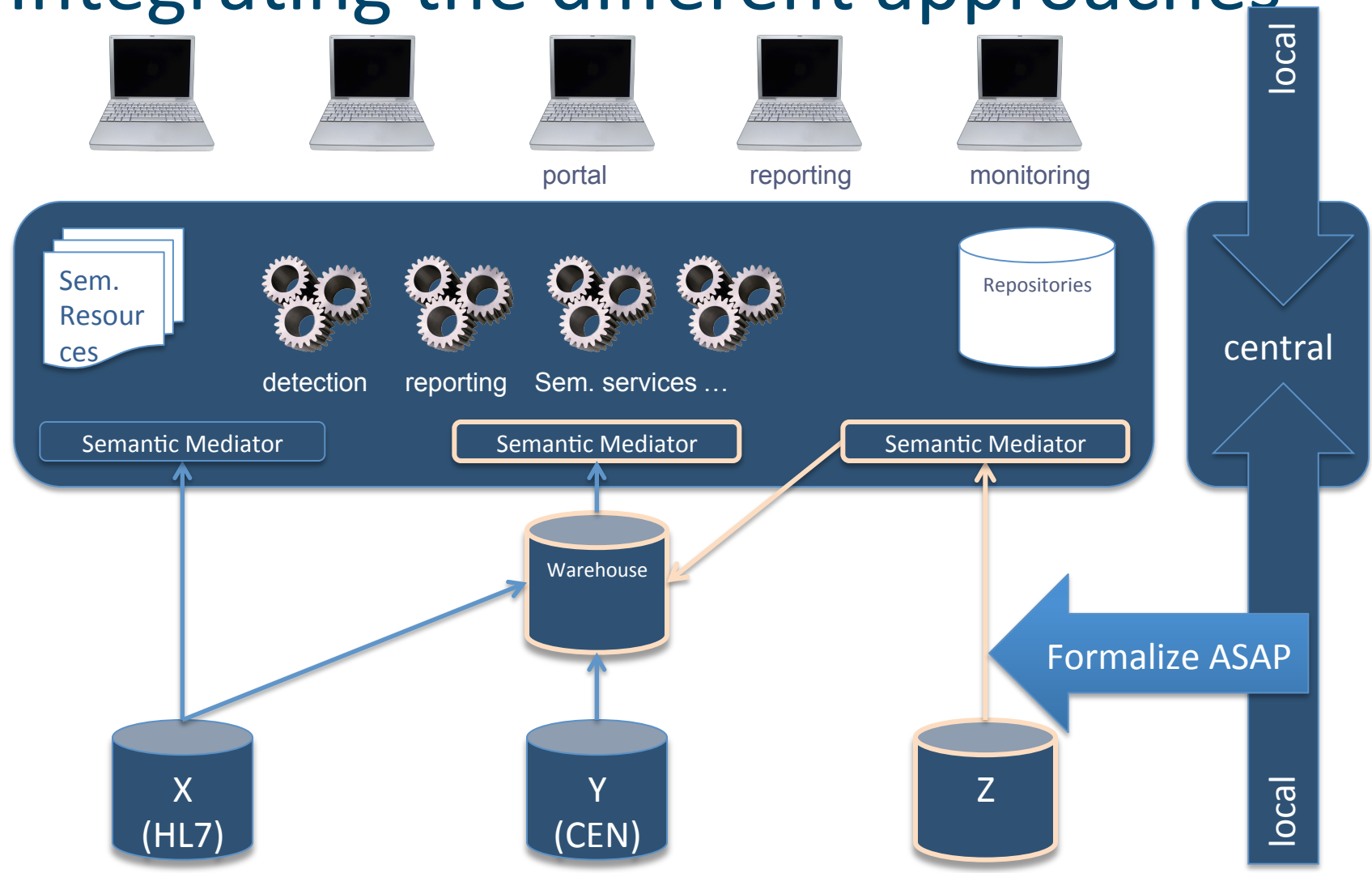
- A simple thing (?) 😊
 - Put a semantic layer on top of any resource
 - Define a common ontology (or a system to mediate between ontologies)
 - Query data as if everything behaves as one virtual system



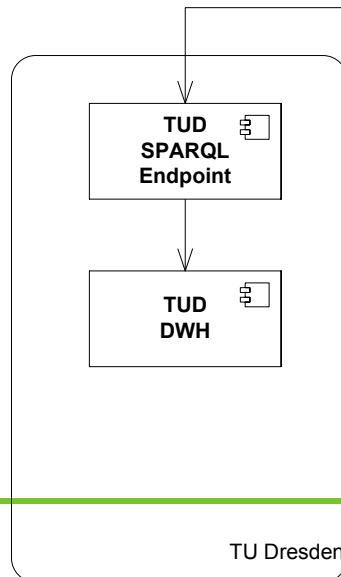
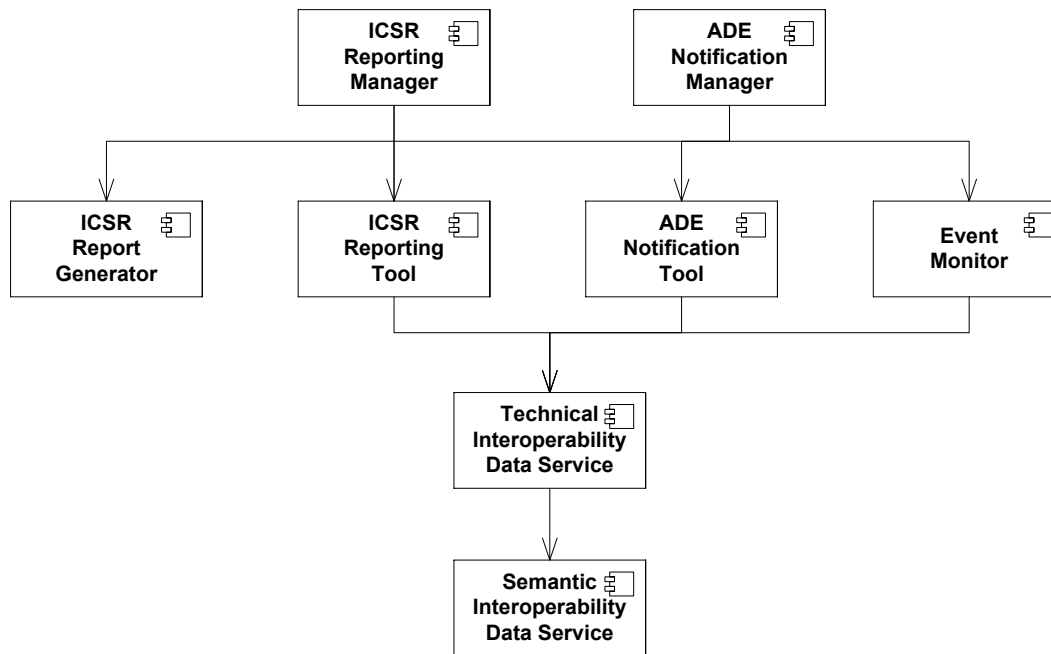
Semantic Interoperability and Service



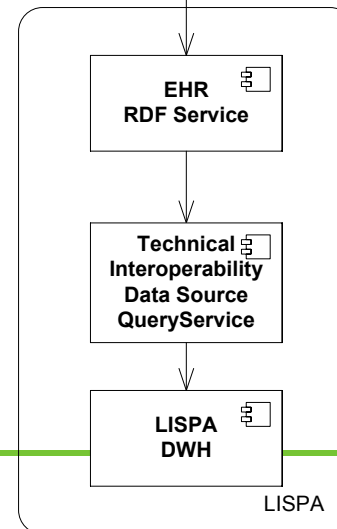
Integrating the different approaches



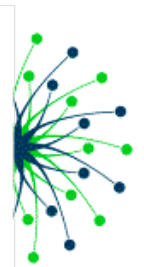
Deployed locally at TU Dresden and at LISPA



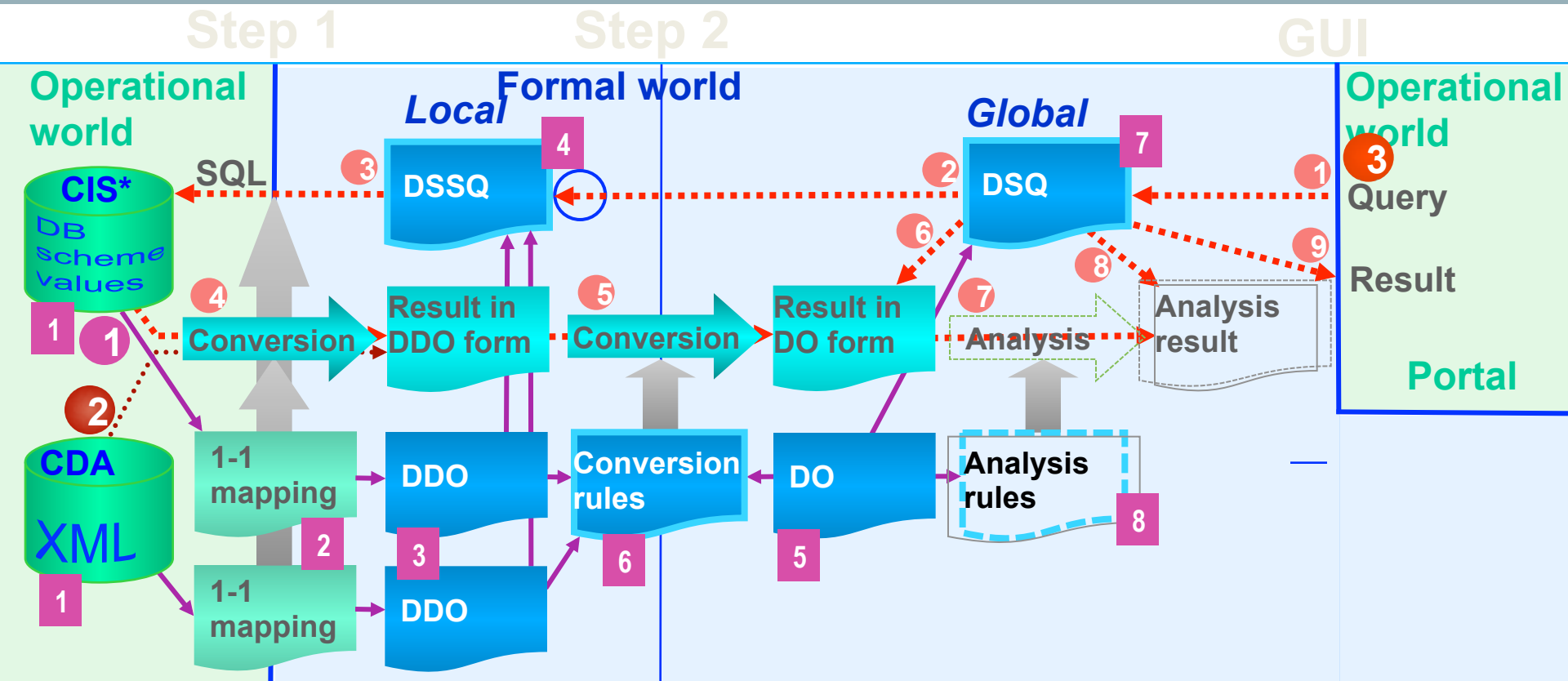
TU Dresden



LISPA



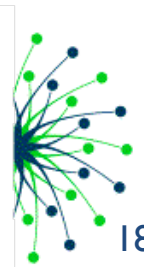
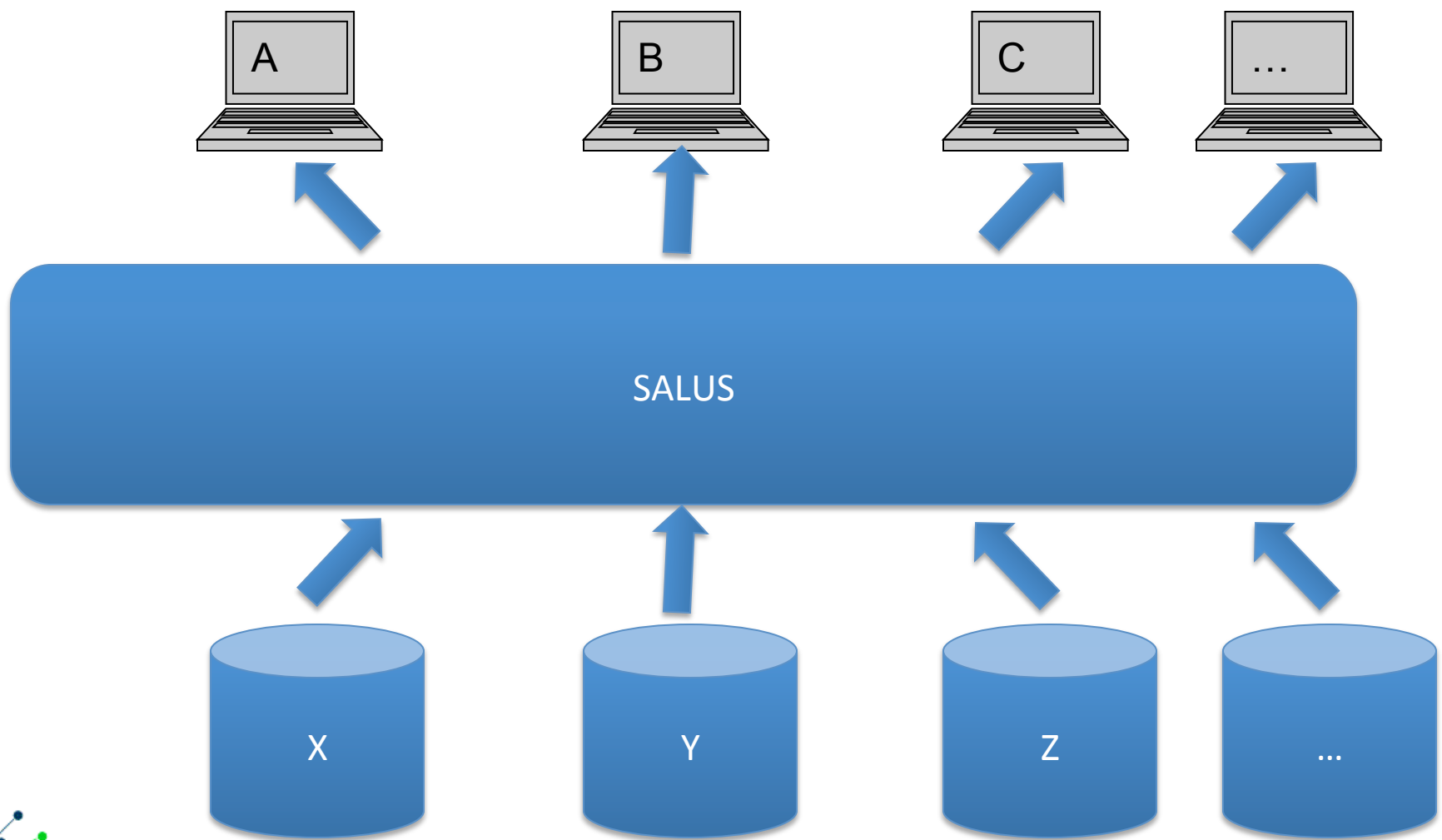
From data to formal resources



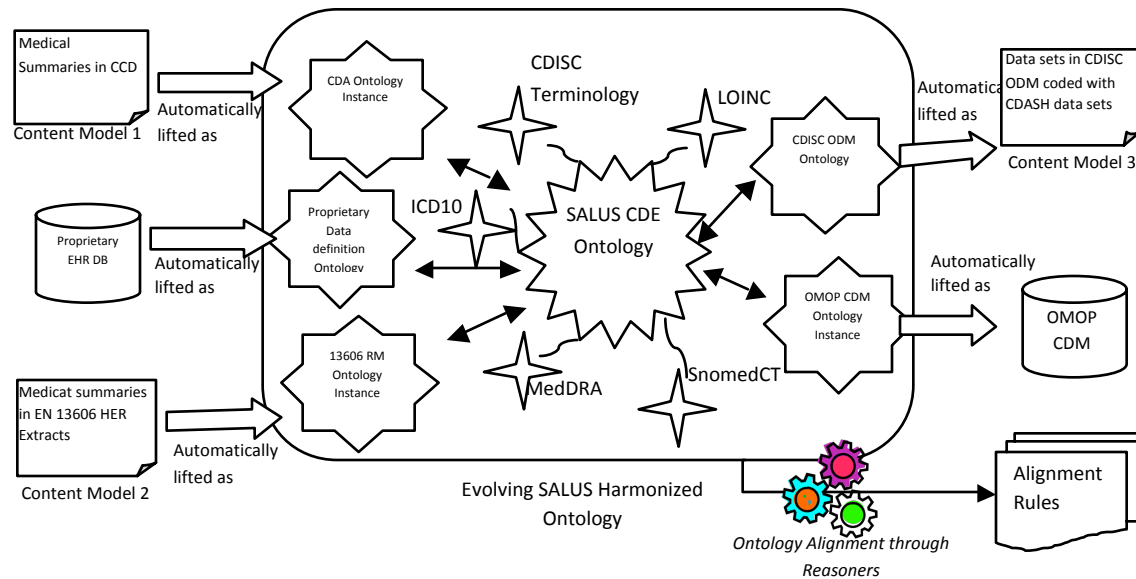
CIS: Clinical Information System
 CTMS: Clinical Trial Management System
 DDO: Data Definition Ontology
 DO: Domain Ontology
 DSQ: Domain SPARQL Query
 DSSQ: Data Set SPARQL Query
 GUI: Graphical User Interface
 SQL: Structured Query Language

- 1** (purple arrow) **At development (deployment) time:** creating "formal library"
- 2** (red arrow) **At any time:** formalizing upfront (triple cache)
- 3** (red arrow) **At runtime:** formalizing (via querying) and deducing (via reasoning with rules)
- Blue box** Using formalisms declared in ontologies

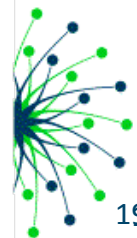
Blue circle Fixed query link



Proposed Semantic Mediation Approach

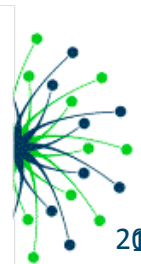


SALUS Semantic Interoperability Platform aims to build a semantic architecture, where data will be mediated to one another through common models, created as a set of semantic resources (common data elements, domain ontologies, terminology systems)



Identification of SALUS common data elements (CDEs)

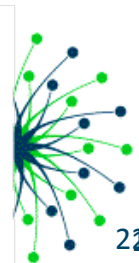
- Collected and merged the different data requirements of our pilot application scenarios
- At the end of this step, we had our Common Data Elements (CDEs) as a matrix



| Selected SALUS Scenarios/Related EHR Sections | Selected SALUS Scenarios/Related EHR Data Items | Enabling Notification of Suspected ADEs | Enabling Semi-automatic ADE Reporting | Characterizing the cases and contrasting them to a background population | Temporal pattern characterization | Running Exploratory Analysis Studies over EHRs for Signal Detection (Temporal Association Screening) | Using EHRs as secondary use data sources for Post Marketing safety studies (Calculating incidence rates of CHF in diabetic patients with a recent acute coronary syndrome (ACS) event) |
|---|---|---|---------------------------------------|--|-----------------------------------|--|--|
| | | | | | | | |
| Patient | Patient Name or Initials | | x (o) | | | | |
| | ID | | | | x (o) (Pseudonym) | | |
| | Date of Birth | x | x (Age is to be derived) | x (Year of Birth is Adequate) | x (Year of Birth is Adequate) | | x (Year of Birth is Adequate) |
| | Gender | x | x (o) | x | x | | x |
| | Race | | x (o) | | x (o) | | |
| | Birth Place (Region or City) | | | | | | |
| | Patient registration date | | | | | x (o) | |
| | Patient de-registration date | | | | | x (o) | |
| | Ethnicity | | x(o) | | x(o) | | |
| | Provider ID | | | | x(o) | | |
| | Provider Organisation ID | | | | x(o) | | |
| | Address | | | | x(o) | | |
| | Investigation number | | x (o) | | | | |
| Pregnancy | YES/NO | x (o) | | | | | |
| | Delivery Date | x (o) | | | | | |
| | Pregnancy Status | x (o) | | | | | |
| | Last Menstrual Period Date | x (o) | x (o) | | | | |
| Condition (Past Medical History) | Problem Name | x(o) | x(o) | x | | x | x |
| | Problem code | x(o) | x(o) | x | x | x | x |
| | Start Date | x(o) | x(o) | x | x | x | x |
| | End Date | x(o) | x(o) | x | x (o) | x | x (o) |
| | Problem Status | x(o) | x(o) | | x | | |
| | Date of Entry | | | x | | x | x |
| | Related Encounter | | | | x (o) | | |
| | Treating Provider | | | | x (o) | | |
| | Severity | x(o) | | | | | |
| | Comments / text describing Problem | | x(o) | | | | |
| Condition (Active Problems/Symptoms) | Problem Name | x | x (o) | x | | x | x |
| | Problem code | x | x (o) | x | x | x | x |
| | Start Date | x | x (o) | x | x | x | x |
| | End Date | x | x (o) | x | x | x | x (o) |
| | Problem Status | x | x (o) | | x | | |
| | Date of Entry | x | | x | | | |
| | Related Encounter | | | | x | | x |
| | Treating Provider | | | | x | | |
| | Severity | x | | | | | |
| | Comments / text describing Problem | | x(o) | | | | |
| Allergies/Intolerance | Adverse Event Type (text) | x (o) | x (o) | x | | x | |

Identification of content models

- Within the scope of Task 4.1, we have identified and presented the content models to be used in SALUS
 - A harmonization of HL7/ASTM CCD, IHE PCC and HL7/IHE/ONC Consolidated CDA templates based on HL7 CDA -> SRDC
 - OMOP Common Data Model (CDM) templates -> SRDC
 - ICH E2B(R2) templates -> INSERM
 - ISO/CEN EN 13606 archetype library -> ERS
- These are able to cover the data requirements of SALUS pilot applications; hence the SALUS CDEs
- Also, provided mappings at the conceptual level between pairs of these standards (e.g. CDA to E2B(R2), CDA to OMOP CDM))



| | |
|--------------------|---|
| Possible Sections: | Past Medical History Section or Active Problems Section //cda:section[cda:templateId/@root='1.3.6.1.4.1.19376.1.5.3.1.3.8' cda:templateId/@root='1.3.6.1.4.1.19376.1.5.3.1.3.6'] |
|--------------------|---|

OR

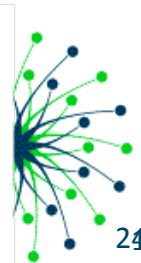
| Location in CDA Document in the specified sections | Common Data Element Name | Cardinality | Data Type |
|---|---|-------------|------------------------------------|
| cda:entry/cda:act[cda:templateId/@root='1.3.6.1.4.1.19376.1.5.3.1.4.5.2']/ cda:entryRelationship[@typeCode='SUBJ']/cda:observation[cda:templateId/@root='1.3.6.1.4.1.19376.1.5.3.1.4.5'] | Condition | | |
| cda:code/ | Problem Type | 1..1 | CD |
| cda:text/ | Comments / text describing Problem | 0..1 | ED |
| cda:statusCode/ | - | 1..1 | CS |
| cda:effectiveTime/low | Start Date | 0..1 | TS or IVL<TS> (for effective Time) |
| cda:effectiveTime/high | End Date | 0..1 | TS or IVL<TS> (for effective Time) |
| cda:value/cda:originalText | Problem Name | 0..1 | ED |
| cda:value/ | Problem Code (can also indicate Death.cause of death) | 1..1 | CD |
| cda:performer | Treating Provider | 0..1 | |
| cda:entryRelationship/cda:observation [cda:templateId/@root '1.3.6.1.4.1.19376.1.5.3.1.4.1.1']/ value/ | Problem Status | 0..1 | CD |
| cda:entryRelationship/cda:observation [cda:templateId/@root '1.3.6.1.4.1.19376.1.5.3.1.4.1.1']/ value/ | Severity | 0..1 | CD |
| cda:entryRelationship[typeCode='CAUS'] /cda:observation/[cda:code /@code = '419620001'] AND cda:code /@codeSystem='2.16.840.1.113883.6.96/'] | Death | 0..1 | |
| cda:effectiveTime | Date of Death | 0..1 | TS |

Xpaths to CCD/PCC elements

Corresponding SALUS Common Data Elements

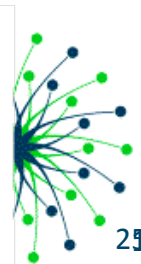
SALUS Draft Common Information Model

- Taking into account the most prominent clinical care standards and initiatives, we have created the SALUS Draft Common Information Model (CIM), which most effectively represents all the CDEs that we have identified
- Similar models that we have analyzed
 - greenCDA representation of HITSP C32 specification,
 - HL7 Clinical Statement Model,
 - hQuery,
 - ASTM CCR,
 - Mini-Sentinel, ...
- We have created the patient-centric SALUS Common Information Model, as an entity model
- It is broad enough to cover not only SALUS requirements
- Yet, it is concise and does not include unnecessary classes that are very specific to clinical trials, etc. (one reason to give up BRIDG DAM)



SALUS Draft Common Information Model - Content

- Patient is the starting point of SALUS Draft CIM, and it covers metadata about the patient:
 - id
 - name, surname, title
 - gender, birth date, birth place, address
 - marital status, race, ethnicity, religion, etc.
- and, medical information:
 - health professionals
 - healthcare providers
 - encounters
 - allergies
 - conditions (problems, diagnoses, etc.)
 - family history
 - immunizations
 - medications
 - pregnancies
 - procedures
 - lab results
 - social history
 - vital signs



How CDEs are created and how they will be used by SIL?

2. Produces content models as HL7 CDA templates, EN 13606 templates, Archetypes, etc. (SIAMS?)

-- This is based on the selected Pilot Scenarios--

Task 4.1
Content Model Creation

Content Models

3. Content Models are imported to CDE Repository as "Content Model Ontologies"

4. "Content Model Ontologies" are annotated with Terminology Codes

5. Matching CDEs are found, "Content Model Ontologies" annotated with these CDEs
If necessary new CDEs are created

Task 4.2
CDE Repository

Task 4.3-4.4 Semantic Mediation Framework

1. Imports existing Domain Models, and domain ontologies as a basis, identifies and maintains CDEs as an ontology conforming to ISO-IEC 11179 Repository Metamodel

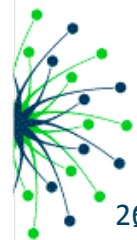
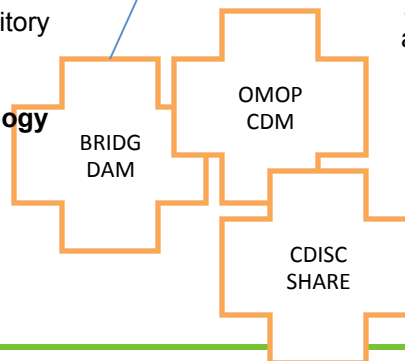
CDEs are annotated with Terminology Codes

6. A part of SALUS Resource Set is created from CDEs

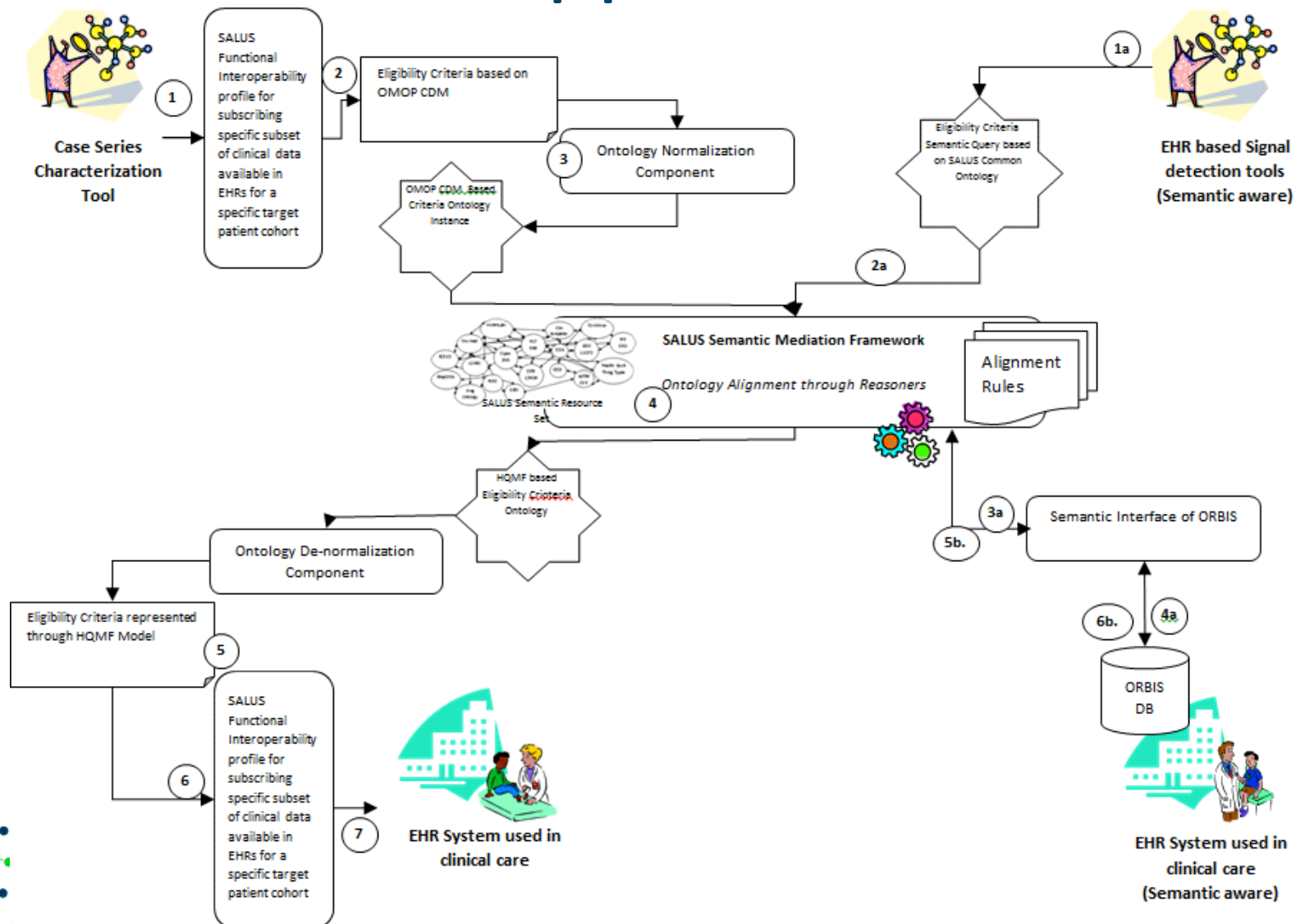
7. Annotated Content Model Ontologies are loaded

8. Using Annotated Content Model Ontologies, "Mapping Definitions" between these and SALUS Semantic Resource Set is created

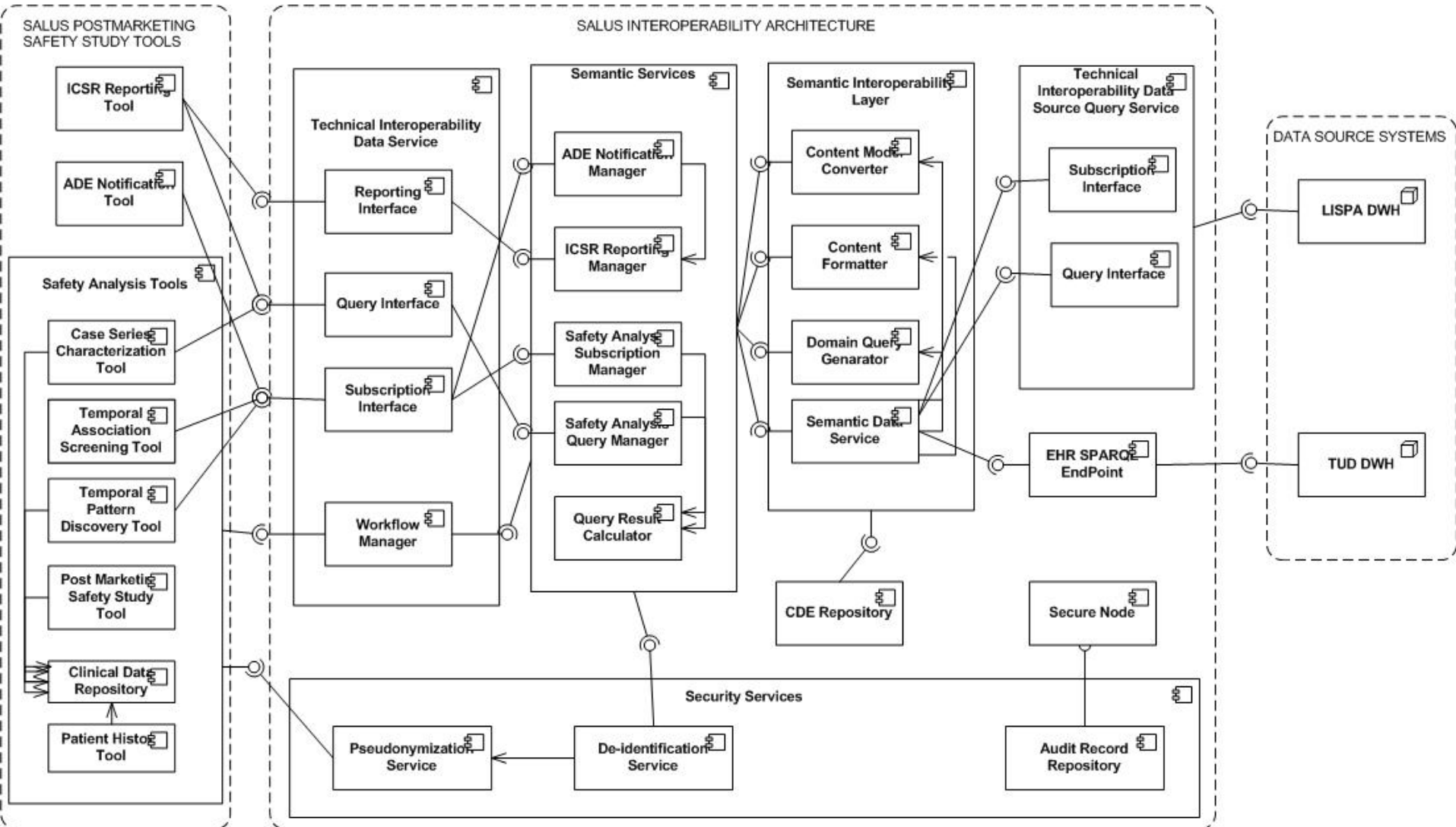
9. Using "Mapping Definitions", Clinical Content represented in Content Models can be semantically mediated to/from SALUS Semantic Resource Set



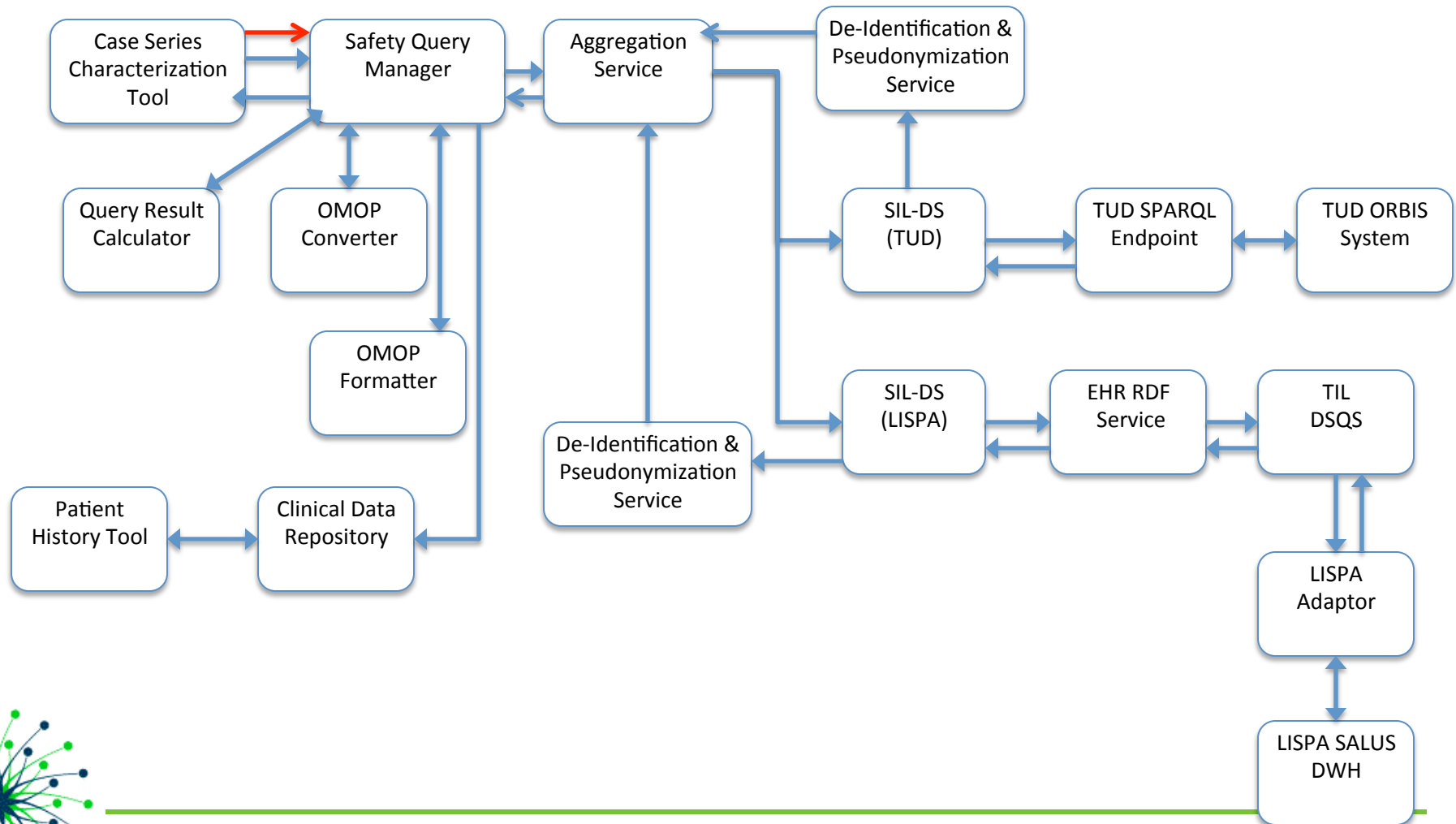
Proposed Semantic Mediation Approach



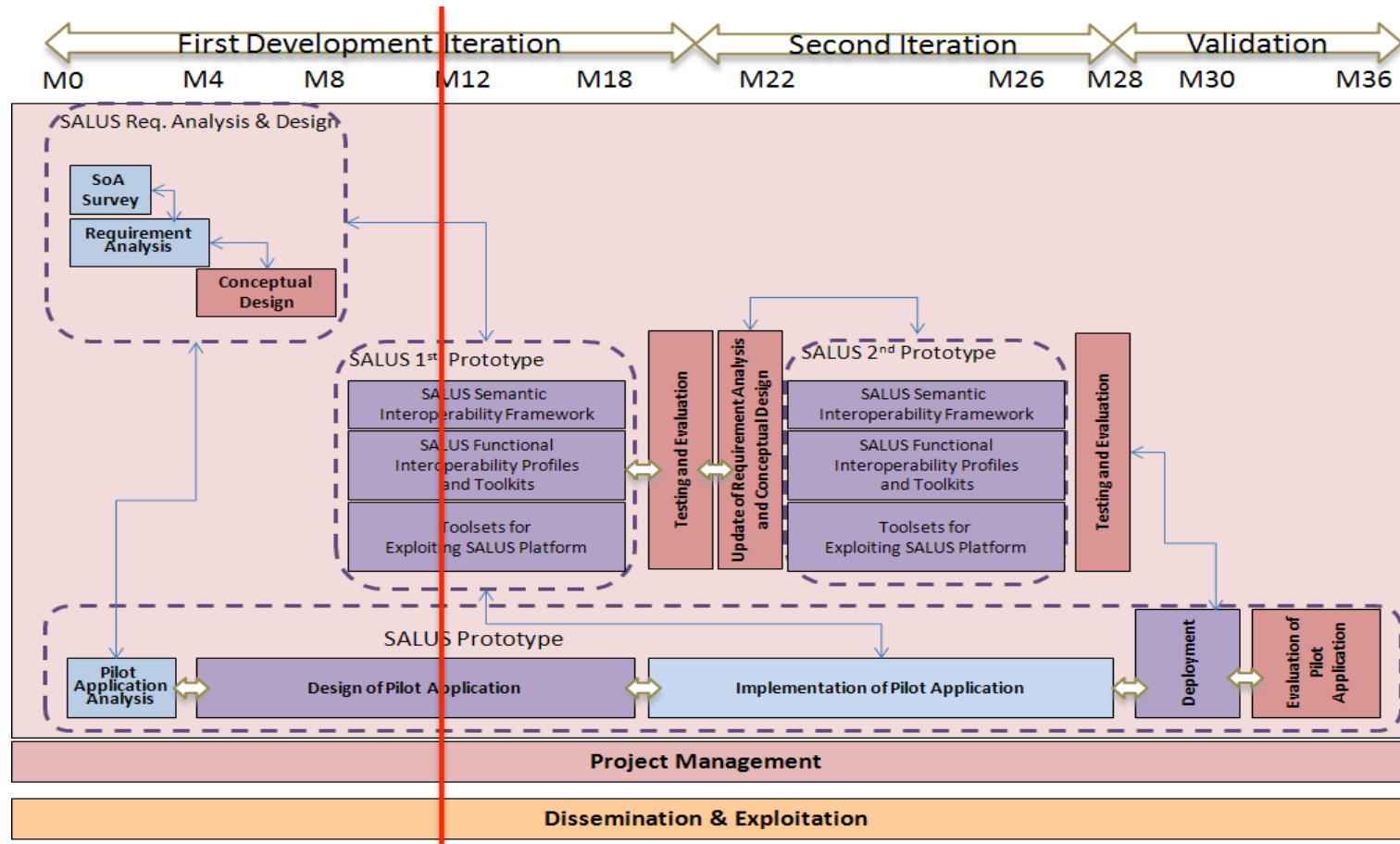
Another Look to WP4-WP5 Interaction



Case Series Characterization revisit



Project timeline



Month1
1,5

January 16, 2013

SALUSTechnic
al Meeting,
Paris, France

Project Information

- <http://www.salusproject.eu/>
- Publications
 - Providing Semantic Interoperability between Clinical Care and Clinical Research Domains, Accepted for publication in IEEE Transactions on Information Technology in BioMedicine
 - SALUS: Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies, MIE 2012, Pisa- Italy, 26-29 August 2012.
 - Building the Semantic Interoperability Architecture Enabling Sustainable Proactive Post Market Safety Studies, Accepted as a poster in SIMI 2012 Wokshop (Semantic Interoperability in Medical Informatics), in ESCW 2012: Extended Semantic Web Conference, May 27, 2012 in Heraklion (Crete), Greece
 - Semantic-sensitive extraction of EHR data to support adverse drug event reporting, SWAT4LS Workshop, Paris - France, 30 November 2012
 - Two MedInfo Submissions
 - One Panel Discussion submission to AMIA Clinical Research Informatics meeting (In cooperation with EHR4CR)
 - ISO/IEC 11179 Metadata Registry implementation has been presented in Apache TCon
- Contact information
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